WIRO 8 JOH THE TOWN

Date

PTO/SB/21 (02-04) Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Inder the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. Application Number 10/663943 TRANSMITTAL Filing Date 09.16.2003 **FORM** First Named Inventor Rolland Hebert Art Unit (to be used for all correspondence after initial filing) **Examiner Name** Attorney Docket Number Total Number of Pages in This Submission **ENCLOSURES** (Check all that apply) After Allowance communication Fee Transmittal Form Drawing(s) to Technology Center (TC) Appeal Communication to Board Licensing-related Papers Fee Attached of Appeals and Interferences Appeal Communication to TC Petition Amendment/Reply (Appeal Notice, Brief, Reply Brief) Petition to Convert to a Proprietary Information After Final Provisional Application Power of Attorney, Revocation Status Letter Affidavits/declaration(s) Change of Correspondence Address Other Enclosure(s) (please Terminal Disclaimer **Extension of Time Request** Identify below): postcoud receip Request for Refund **Express Abandonment Request** CD, Number of CD(s) Information Disclosure Statement Remarks Certified Copy of Priority Document(s) Response to Missing Parts/ Incomplete Application Response to Missing Parts under 37 CFR 1.52 or 1.53 SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT Firm Rolland Hebert Individual name Signature

## CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

| Signature             | Mtebert        | Date | 2/21/04 | _ |
|-----------------------|----------------|------|---------|---|
| Typed or printed name | Rolland Hebert |      |         |   |

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03) Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| Substitut | e for form 1449/PTO                     |          |           |                        | n of information unless it contains a valid OMB control number.  Complete if Known |
|-----------|---|----------|-----------|------------------------|--|
| Cobound   | 0.00.0000000000000000000000000000000000 |          |           | Application Number     | 10/663943  |
| INFO      | DRMATION                                | I DIS    | CLOSURE   | Filing Date            | 09-16-2003   |
| STA       | TEMENT E                                | BY A     | PPLICANT  | First Named Inventor   | Rolland Hebert   |
|           | (line on monumb                         |          |           | Art Unit               |  |
|           | (Use as many she                        | ets as n | ecessary) | Examiner Name          |  |
| Sheet     | 1                                       | of       | 2         | Attorney Docket Number |  |

|                       |                          | NON PATENT LITERATURE DOCUMENTS   |                |
|-----------------------|--------------------------|---|----------------|
| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|                       |                          | BORCHARDT RT and WU YS , Potential inhibitors of S-adenosylmethionine-dependent methyltransferases. Role of the Asymmetric Sulfonium Pole in the Enzymatic binding of S-adenosy   |                |
|                       |                          | BOTTIGLIERI et al (1994), The Clinical Potential of Ademetionine (S-adenosylmethionine) in neurological disorders, Drugs, 48 (2), 137-152.US  |                |
|                       |                          | CHENG et al, (1997), Levels of L-methionine S-adenosyltransferase activity in erythrocytes and concentrations of S-adenosylmethionine and S-adenosylhomocysteine in whole blood   |                |
|                       |                          | DE LA CRUZ et al, (2000), Effects of chronic administration of S-adenosyl-l-methionine on brain oxidative stress in rats. Naunyn-Schmiedeberg's Archives Pharmacol 361: 47-52.U   |                |
|                       |                          | DE LA HABA et al. The relation of Configuration at the Sulfonium Center to Enzymatic Reactivity. J. Am. Chem. Soc. 81, 3975-3980, 1959  |                |
|                       |                          | DETICH et al "The methyl donor S-adenosyl-l-methionine inhibits active demethylation of DNA; a candidate novel mechanism for the pharmacological effects of S-adenosylmethion   |                |
|                       |                          | DI PADOVA C, (1987), S-adenosyl-l-methionine in the treatment of osteoarthritis: review of the clinical studies. Am J. Med. 83, (Suppl. 5), 6-65 US   |                |
|                       |                          | FRIEDEL et al, S-adenosyl-l-methionine: A review of its pharmacological properties and therapeutic potential in liver dysfunction and affective disorders in relation to its ph   |                |
|                       |                          | GALAN A, et al, Cyclosporine A toxicity and effect of the s-adenosylmethionine, Ars Pharmaceutica, 40:3; 151-163, 1999.   |                |
|                       |                          | HOFFMAN J, Chromatographic Analysis of the Chiral and Covalent Instability of S-adenosyl-I-methionine, Biochemistry 1986, 25 4444-4449 US   |                |

| Examiner  | Date       |  |
|-----------|------------|--|
| Signature | Considered |  |

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The Information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03) Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

|                        | te for form 1449/PTC |             |           | required to respond to a collection of information unless it contains a valid OMB control number.  Complete if Known |                |  |  |  |
|------------------------|----------------------|-------------|-----------|--|----------------|--|--|--|
|                        |                      |             |           | Application Number   | 10/663943      |  |  |  |
| INF                    | ORMATIO              | N DIS       | CLOSURE   | Filing Date  | 09.16.2003     |  |  |  |
| STATEMENT BY APPLICANT |                      |             |           | First Named Inventor   | Rolland Hebert |  |  |  |
|                        | **                   |             |           | Art Unit   |                |  |  |  |
|                        | (Use as many s       | heets as ne | ecessary) | Examiner Name  |                |  |  |  |
| Sheet                  | 2                    | of          | 2         | Attorney Docket Number   | <u> </u>       |  |  |  |

|                       |                          | NON PATENT LITERATURE DOCUMENTS   |                |
|-----------------------|--------------------------|---|----------------|
| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|                       |                          | KAGAN, B, Sultzer D. L., Rosenlicht N and Gerner R. (1990), Oral S-adenosylmethionine in depression: a randomized, double blind, placebo-controlled trial. Am. J. Psychiatry 14   |                |
|                       |                          | KEATING et al (1991), Evidence of brain methyltransferase inhibition and early brain involvement in HIV positive patients Lancet: 337:935-9 UK  |                |
|                       |                          | KOENIG B. A long-term (two years) clinical trial with S-adenosylmethionine for the treatment of osteoarthritis. The American Journal of Medicine, Vol 83 (suppl 5A), Nov. 20, 1   |                |
|                       |                          | MATO et al (1999), S-adenosylmethionine in alcohol liver cirrhosis: a randomized, placebo-controlled, double blind, multi-center clinical trial, Journal of Hepatology, 30, 108   | ·              |
|                       |                          | MATOS, JR, Rauschel FM, Wong, CH. S-Adenosylmethionine: Studies on Chemical and Enzymatic Synthesis. Biotechnology and Applied Biochemistry 9, 39-52 (1987) US  |                |
|                       |                          | MORRISON et al, (1996), Brain S-adenosylmethionine levels are severely decreased in Alzheimer's disease, Journal of Neurochemistry, 67, 1328-1331. US   |                |
|                       |                          | SEGAL D and Eichler D, The Specificity of Interaction between S-adenosyl-l-methionine and a nucleolar 2-0-methyltransferase, Archives of Biochemistry and Biophysics, Vol. 275,   |                |
|                       |                          | TAVONI et al, Evaluation of S-adenosylmethioine in Primary Fibromaylgia. The American Journal of Medicine, Vol 83 (suppl 5A), pp 107-110, 1987. US  |                |
|                       |                          | VENDEMIALE G et al, (1989), Effect of oral S-adenosyl-l-methionine on hepatic glutathione in patients with liver disease. Scand J Gastroenterol; 24: 407-15.  |                |
|                       |                          | WATSON WH, Zhao Y, Chawla RK, S-adenosylmethionine attenuates the lipopolysaccharide-induced expression of the gene for tumour necrosis factor alpha. (1999) Biochem J Aug. 15;   |                |

| Examiner  | Date       |  |
|-----------|------------|--|
| Signature | Considered |  |

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| Substitute for form 1449/PTO |            |          |          |
|------------------------------|------------|----------|----------|
|                              | Substitute | for form | 1//0/DTO |

Sheet

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

| Complete if Known      |                |  |  |  |
|------------------------|----------------|--|--|--|
| Application Number     | 10/663943      |  |  |  |
| Filing Date            | 09/06/2003     |  |  |  |
| First Named Inventor   | Rolland Hebert |  |  |  |
| Art Unit               |                |  |  |  |
| Examiner Name          |                |  |  |  |
| Attorney Docket Number |                |  |  |  |

|                       |              |  | U. S. PATENT                   | DOCUMENTS  |   |
|-----------------------|--------------|--|--------------------------------|--|---|
| Examiner<br>Initials* | Cite<br>No.1 | Document Number  Number-Kind Code <sup>2 (# known)</sup> | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines, Where<br>Relevant Passages or Relevant<br>Figures Appear |
|                       |              | <sup>US-</sup> 2969353                                   | 01-24-1961                     | Shrink et al                                       | all   |
| ··                    |              | us- 3707536  | 12-26-1972                     | Haid et al   | all   |
|                       |              | us- 3893999  | 07-08-1978                     | Fieceli.   | au  |
|                       |              | <sup>US-</sup> 3954726                                   | 05-04-1976                     | Fiecchi  | all   |
|                       |              | <sup>US-</sup> 4028183                                   | 06-07-1977                     | Fiecchi  | all   |
|                       |              | <sup>US-</sup> 4057686                                   | 11-08-1977                     | Fiecchi  | all   |
|                       |              | <sup>US-</sup> 4109079                                   | 08-22-1978                     | Kawahara   | all   |
|                       |              | us- 4369177  | 01-08-1983                     | Kozaki   | all   |
|                       |              | <sup>US-</sup> 4465672                                   | 08-14-1984                     | Gennari  | all   |
|                       |              | <sup>US-</sup> 4543408                                   | 09-24-1985                     | Gennari  | all   |
|                       |              | <sup>US-</sup> 4558122                                   | 12-10-1985                     | Gennari  | all .   |
|                       |              | <sup>US-</sup> 4764603                                   | 08-16-1988                     | Zappia   | all   |
|                       |              | <sup>US-</sup> 4990606                                   | 02-05-1991                     | Gennari  | all   |
|                       |              | us- 5073546  | 12-17-1991                     | Zappia   | all   |
|                       |              | us- 5102791  | 04-07-1992                     | Zappia   | all   |
|                       |              | US- 5114931  | 05-19-1992                     | Gennari  | all   |
|                       |              | <sup>US-</sup> 5128249                                   | 07-07-1992                     | Gennari  | all   |
|                       |              | <sup>US-</sup> 5137712                                   | 08-11-1992                     | Kask   | all   |
|                       |              | <sup>US-</sup> 5196402                                   | 03-23-1993                     | Braganza   | all   |

| FOREIGN PATENT DOCUMENTS |              |   |                     |  |   |    |  |  |
|--------------------------|--------------|---|---------------------|--|---|----|--|--|
| Examiner<br>Initials*    | Cite<br>No.1 | Foreign Patent Document   | Publication<br>Date | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines,<br>Where Relevant Passages | Π  |  |  |
|                          |              | Country Code <sup>3</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known) | MM-DD-YYYY          | , фрисант от сисс 2000 и                           | Or Relevant Figures Appear                        | Τ' |  |  |
|                          | <u> </u>     |   |                     |  |   |    |  |  |
| _                        |              |   |                     |  |   |    |  |  |
|                          |              |   |                     |  |   |    |  |  |
|                          |              |   |                     |  |   | Ĺ  |  |  |
|                          |              |   |                     |  |   |    |  |  |
|                          | T            |   |                     |  |   | Г  |  |  |

|           |            | <br> |
|-----------|------------|------|
| Examiner  | Date       |      |
| Signature | Considered |      |
|           |            |      |

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.